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No. 03-443

IN THE

Supreme Court of the United States

ALLERGAN, INC. AND ALLERGAN SALES, INC.,
Petitioners,

v.

ALCON LABORATORIES, INC., ALCON RESEARCH LTD., ALCON UNIVERSAL, LTD., AND BAUSCH & LOMB INCORPORATED,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

REPLY BRIEF IN SUPPORT OF PETITION

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REPLY BRIEF IN SUPPORT OF PETITION

Respondents and their *amicus* argue that the decision below is not worthy of review because there is no split of authority over the issue presented. But that cannot be the standard where, as here, the Federal Circuit has exclusive jurisdiction over an issue. Rather, this Court has made clear that it will grant review of such cases where the issue is important, there is a clear division of views within the Federal Circuit, and there is strong evidence that the issue was decided incorrectly. All three factors are plainly present here.

Nor is there any merit to the claim that a recent Food and Drug Administration ("FDA") regulation renders the issue presented unimportant. That regulation is based on the same erroneous decisions that are the subject of this petition. The fact that the Federal Circuit's misconstruction of § 271(e)(2) has now infected regulations implementing other provisions of the statute underscores the need for this Court's review.

1. As petitioner has shown, the proper interpretation of § 271(e)(2) has profound implications for the public's health and welfare. By ruling that § 271(e)(2) does not protect patents that cover either "off-label" uses or only one of several uses approved by the FDA, the Federal Circuit has effectively destroyed the incentives for discovering and developing new, potentially life-saving uses of existing drugs. Respondents have completely failed to refute this showing.

The harms to innovation that the decision below will cause result from several indisputable realities of the drug industry. First, discovering and developing new uses for existing drugs is a time-consuming and expensive endeavor. Pet. 15. Patent protection is thus essential to fostering such development efforts. Second, physicians can and often do prescribe drugs for uses other than those the FDA has approved; indeed, "off-label" use is frequently state-of-the-art medicine. *Id.* at 6-7. As a result, where a pioneer develops a commercially

valuable, patented new use for an existing drug, generic manufacturers can seek FDA approval for a previously approved use knowing the drug can be prescribed for the patented, off-label use. Where a generic manufacturer induces physicians to prescribe its drug for an infringing off-label use, the pioneer suffers an immediate and enormous loss of the profits necessary to recoup its research and development investment. *Id.* at 16.

The purpose of this lawsuit was to prevent precisely this type of injury. Without any discovery, petitioner adduced enough publicly available evidence "to present a triable issue of fact" concerning respondent Alcon's induced infringement, "or at the least [to] allow [petitioner] to conduct discovery." Pet. App. 53a. Nontheless, petitioner's suit was dismissed because the Federal Circuit had concluded in a prior opinion that § 271(e)(2) cannot be used to prevent the harm of induced infringement by an ANDA holder, no matter how much evidence of such harm the patentee presents.[1]

Respondents now blithely assert that "all of the traditional remedies for patent infringement are still available to . . . patent holders [such as petitioner], which provide more than enough incentive for them to research new uses of existing drugs." B&L Opp. 2; see also Alcon Opp. 21 (patentee can "enforce a method-of-use patent after the FDA approves" an ANDA); GPhA Br. 10 (same). But respondents nowhere address, let alone refute, petitioner's showing that, once an ANDA is approved and physicians begin prescribing the generic drug for off-label use, it is virtually impossible to obtain a preliminary injunction barring such use. Pet. 16-17. Respondents likewise fail to address petitioner's showing that a post-infringement damages remedy is inadequate because

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[1] Thus, respondents' arguments about the supposed inadequacies of the record regarding off-label use of brimonidine for neuroprotection, respondents' awareness of that use, and their intent to induce such use, *see* Alcon Opp. 7 n.4, 8 n.5; B&L Opp. 8-9, are utterly irrelevant.

generic manufacturers typically lack the assets necessary to restore the pioneer's lost profits. *Id.* at 17.

Contrary to B&L's claim, these are *not* harms that could befall "any patent holder." B&L Opp. 13. Because drugs, like medical devices, are essential to promoting health and saving lives, those who hold patents on methods of using drugs face unique public policy barriers to preliminary injunctive relief, regardless of the strength of their cases on the merits. Pet. 17 n.5. Similarly, because of the very large disparity in the capitalization of pioneers, who make huge investments in research and development, and most generic manufacturers, who free-ride on those investments, pioneers are uniquely unlikely to collect full compensation from infringers. These unique harms cannot be brushed aside with assurances that generic manufacturers are unlikely to infringe at all, B&L Opp. 13, as the facts of this very case show.

Nor is true that patent term restoration alone provides adequate incentives for innovation. GPhA Br. 9. Term restoration merely compensates for years of patent protection lost during clinical testing and the NDA review process. Before that testing and review can even begin, however, pioneers must first discover and develop new uses for existing drugs. Such breakthroughs require enormous investments, Pet. 15. Yet, under the Federal Circuit's crabbed reading of § 271(e)(2), pioneers have no way of recouping these very investments, which the patent laws are designed to foster.

It is no answer to suggest that pioneers can protect such investments by obtaining NDAs on their new uses. GPhA Br. 9. Once the FDA approves an NDA for an initial use of a drug, manufacturers can submit ANDAs for just that initial use. After such ANDAs are granted, however, physicians can prescribe the generic for any use. Thus, once the generic enters the market, a pioneer's exclusive right to label for a second, FDA-approved use is meaningless: physicians can and will prescribe the generic for the second approved use, even though the ANDA did not approve the generic for that

use. See Pet. 17-18.[2] For the reasons recited above, moreover, any infringement action brought after the generic enters the market is a wholly inadequate remedy.

Unlike respondents, Congress recognized these harms, which is why the Hatch-Waxman Act's patent-related provisions ensure that infringement disputes regarding a generic drug covered by a valid use patent are resolved before the FDA gives marketing approval to the generic. Pet. 4-5, 18-19. Because the Federal Circuit's binding interpretation of § 271(e)(2) frustrates this scheme and irrefutably destroys the incentives necessary to discover and develop new uses of existing drugs, the issue presented is an exceptionally important one. Indeed, its importance is confirmed by the lengthy criticisms leveled at the *Warner-Lambert* decision by the panel below, by the criticisms the Federal Trade Commission leveled at the district court decision below, and by the participation of *amici*, including the generic drug trade association, at the petition stage of this case. This Court's review of such an important issue is plainly warranted.

2. The clear divergence of views within the Federal Circuit over the proper interpretation of § 271(e)(2) is an additional factor that counsels strongly in favor of review. See Pet. 19-20 (citing cases in which this Court has noted divergence of views in the Circuit when granting certiorari). The suggestion that the lack of dissent from the denial of rehearing below somehow reflects unanimity in the Federal Circuit, or a belief that the issue is unimportant, B&L Opp. 11; Alcon Opp. 11, 23; GPhA Br. 5, is frivolous. The panel members below took the remarkable step of detailing the analytical flaws in the *Warner-Lambert* decision and explaining why it frustrated Congress's intent. Their failure to repeat this showing in

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[2] These realities, not some nefarious "strategi[c] deci[sion]," GPhA Br. 9, led petitioner not to seek an NDA for neuroprotective use of brimonidine.

dissents on rehearing in no way reflects a retreat from their prior, published criticisms.[3]

3. Respondents' attempts to rebut those criticisms likewise provide no basis for denying review. As petitioner has shown, the *Warner-Lambert* panel engaged in an undisguised amendment of the statute. It read the statutory phrase "[an ANDA] for a drug . . . the use of which is claimed in a patent," 35 U.S.C. § 271(e)(2)(A), to mean "[an ANDA] for a drug . . . the use of which is claimed in a patent *and is listed in the ANDA*." See *Warner-Lambert Co.* v. *Apotex Corp.*, 316 F.3d 1348, 1356 (Fed. Cir. 2003). Respondents reiterate *Warner-Lambert*'s assertion that the phrase "*the* use . . . claimed in a patent" must refer to the use "listed in the ANDA" because that is the only use the FDA can approve. B&L Opp. 15; Alcon Opp. 13. But this is a question-begging tautology. Although a generic can be approved only for the use "listed in the ANDA," it can be prescribed for other uses and can thereby infringe patents claiming off-label uses. The scope of the FDA's approval authority, therefore, says nothing whatever about whether Congress intended to permit § 271(e)(2) actions for such patents. An intent to foreclose such actions cannot be inferred from Congress's decision to use the phrase "the use" instead of the phrase "a use."

Moreover, despite their insistence that the phrase "the use" be read in context, respondents—like the *Warner-Lambert* panel—fail to address other provisions of the Hatch-Waxman Act that squarely refute such a reading. First, in authorizing patent term restoration, the Act provides that, for use patents, any restoration must be "limited to any use claimed by the patent *and approved for the [drug]*." 35 U.S.C. § 156(b)(2)

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[3] The fact that rehearing was not sought in *Warner-Lambert*, B&L Opp. 16 n.2., is irrelevant. Unlike petitioner, Warner-Lambert failed to proffer adequate evidence of inducement to prevail under any interpretation of § 271(e)(2). *See* Pet. App. 26a (Schall, J., concurring). Accordingly, seeking rehearing would have been a vain act for Warner-Lambert.

(emphasis added). Thus, Congress plainly knew how to specify uses that are both "claimed" in a patent and "approved" by the FDA. The fact that it did so in other provisions of the very same Act, but not in § 271(e)(2), is fatal to any effort to read the additional qualification of an "approved" use into the latter provision. See, *e.g.*, *Russello* v. *United States*, 464 U.S. 16, 23 (1983).

Second, the *Warner-Lambert* panel's interpretation is flatly contradicted by the Act's certification and statement provisions. These provisions require an ANDA filer to make one of four certifications for a patent "which claims a use for [the] listed drug," including, if applicable, a certification

> (IV) that such patent is invalid or *will not be infringed* by the manufacture, use, or sale of the new drug for which [the ANDA] is submitted, *and*
>
> (viii) if with respect to the listed drug . . . information was filed . . . for a method of use patent *which does not claim a use for which the applicant is seeking approval under this subsection*, a statement that the method of use patent does not claim such a use.

21 U.S.C. § 355(j)(2)(A)(vii) & (viii) (emphases added). The conjunctive "and" makes indisputably clear that, even where a listed method of use patent "does not claim a use for which the applicant is seeking approval," an ANDA filer must submit *both* a paragraph (IV) certification *and* a subsection (viii) statement. Because a paragraph (IV) certification is the triggering event for a § 271(e)(2) action, and because the Act requires such certifications even where the listed patent does not claim the use for which approval is sought, § 271(e)(2) cannot be construed to bar suit whenever a use patent does not claim the use listed in the ANDA.

Respondents and their *amicus* do not even address these showings. Instead, Alcon claims that its fatally flawed reading is confirmed by the patent listing provision, which requires NDA applicants to submit information on "any

patent . . . which claims a method of using [the] drug and with respect to which a claim of patent infringement could reasonably be asserted." 21 U.S.C. § 355(b)(1). According to Alcon, "the *only* patents" that "could *reasonably* be asserted in the ANDA context"—and thus the only patents that should be listed—"are patents which claim the use for which an ANDA seeks approval." Alcon Opp. 16 (first emphasis added). But, as just noted, Congress *expected* NDA applicants to list patents that do *not* cover FDA approved uses. See 21 U.S.C. § 355(j)(2)(A)(viii) (requiring statement when "information was filed under [the listing provision] . . . or a method of use patent which does not claim a use for which the applicant is seeking approval"); see also *Apotex, Inc.* v. *Thompson*, No. 02-1295, 2003 WL 224277722, at *7 (Fed. Cir. Oct. 27, 2003) (under the listing provision, use patents should be listed "if it is reasonable to conclude that a person who makes, uses, or sells the drug would infringe").[4] And, as petitioner and Judge Schall have shown, patents on off-label uses *can* "reasonably be asserted" against ANDA filers who actively induce post-approval infringement.

Thus, both the plain language of § 271(e)(2) and its statutory context confirm that a patentee can bring an infringement action upon the filing of an ANDA "for a drug . . . the use of which is claimed in a patent," whether or not the ANDA seeks approval for the patented use. Neither the Act's purposes nor its legislative history remotely justify a departure from this plain meaning.[5] See, *e.g.*, *Garcia* v.

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[4] If Congress believed that only use patents claiming approved uses could be asserted in the ANDA context, it would have simply required the listing of use patents that claim "the method of using the drug specified in the NDA," since those are the only uses for which an ANDA applicant can seek approval.

[5] The existence of *Warner-Lambert*'s mistaken interpretation does not, as Alcon claims, Alcon Opp. 14, render § 271(e)(2) ambiguous. *See, e.g.*, *Ingalls Shipbuilding, Inc.* v. *Director, Office of Workers' Comp. Programs*, 519 U.S. 248, 254-55, 261 (1997) (granting review to resolve

United States, 469 U.S. 70, 75 (1984) ("the most extraordinary showing of contrary intentions" is required to override plain language). In fact, both are consistent with the interpretation that the panel below would have adopted.

Giving § 271(e)(2) its plain meaning does not frustrate Congress's intent to foster legitimate generic competition. Contrary to the claims of respondents (and the *Warner-Lambert* panel), pioneers cannot "strangle generic competition" simply by acquiring narrow patents on off-label uses and using them to block ANDAs seeking approval for different uses. Alcon Opp. 22; see also B&L Opp. 16. Rather, owners of such patents must be able to allege in good faith, and to prove, not only that the generic drug could be prescribed for the patented use, but also that the ANDA applicant *is affirmatively inducing that infringing use*. See Pet. App. 26a (Schall, J., concurring) (petitioner stated a valid claim because it alleged that respondents were "promot[ing]" infringing uses).[6] Thus, pioneers can employ method of use patents as "swords" *only* against generic manufacturers who engage in illegal competition. There is nothing "absurd" about barring those who seek to compete illegally from entering the market, and doing so will not bar entry by others who do not induce unlawful infringement.[7]

Nor do references in the House Report to "controlling use patents"—*i.e.*, those that claim the use specified in the

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circuit split on meaning of statute and concluding the plain language controlled); *see also Reno* v. *Koray*, 515 U.S. 50, 64 (1995) ("A statute is not ambiguous for purposes of lenity merely because there is a division of judicial authority over its proper construction.") (internal quotation marks omitted).

[6] Accordingly, liability can be imposed in a § 271(e)(2) suit based only on intentional inducement and not, as B&L hysterically claims, on a "strict liability standard . . . for all infringing off-label uses." B&L Opp. 13.

[7] It also will not enable petitioner to "retain the exclusive rights to all uses of" brimonidine, including an unpatentable use. Alcon Opp. 21.

NDA—justify *Warner-Lambert*'s refusal to give § 271(e)(2) its plain meaning. The Report does *not* state that "controlling use" patents are the "only" use patents for which a certification is ever required, as respondents misleadingly claim. See Alcon Opp. 17. Indeed, the fact that Congress understood the concept of "controlling use" patents but did not use that concept in the statute itself undermines any effort to imply such a limitation in § 271(e)(2). See Pet. App. 24a (Schall, J., concurring). Moreover, the Report explains that where a drug is approved for two indications and an ANDA seeks approval "only for Indication No. 1, and not Indication No. 2 because it is protected by a use patent, then the applicant must make the appropriate certification and a statement explaining that it is not seeking approval for Indication No. 2." H.R. Rep. No. 98-857, pt. 1, at 22 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2655. In this example, any use patent claiming indication No. 2 is not a "controlling" use patent because it does not claim the use for which the applicant seeks approval (indication No. 1). Nevertheless, the Report explains that the ANDA filer must make both an "appropriate certification" and a statement concerning the non-"controlling use" patent, which is consistent with the Act's certification and statement provisions. See *supra* at 7.[8]

4. Finally, there is no merit to respondents' claim that the FDA's recent amendment of its patent listing regulations strips the Federal Circuit's interpretation of § 271(e)(2) of any continuing legal importance. In explaining why it was limiting Orange Book listings to method of use patents "that claim indications or other conditions of use that are described in the pending or approved [NDA]," Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,704 (June 18, 2003) (to be codified at 21 C.F.R. § 314.53(b)), the FDA expressly relied on the very same erroneous Federal

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[8] The Report's reference to an "appropriate certification" distinguishes between the four mutually exclusive certifications set out in paragraphs (I) through (IV), not between the two use patents in the example.

Circuit decisions that are the subject of this petition. See *id.* at 36,681-82 (citing *Warner-Lambert* and the per curiam decision in this case as support for its regulation). The importance of the issue presented by this case—and the necessity of review by this Court—is thus underscored, not diminished, by the fact that a federal agency has relied on the lower court's erroneous interpretation in implementing a related statutory provision.

Indeed, had the Federal Circuit interpreted § 271(e)(2) correctly in *Warner-Lambert* and in this case, the FDA could not have issued a regulation limiting Orange Book listings to use patents that claim only FDA-approved uses. Faced with a judicial determination that patents claiming off-label uses *can* be enforced in § 271(e)(2) actions, the FDA would have had to permit the listing of patents claiming such uses. Otherwise, the judicially recognized right to enforce such patents under § 271(e)(2) would have been rendered nugatory by an agency that has no authority to interpret or implement that provision.

In short, it is the Federal Circuit's erroneous interpretation of § 271(e)(2) that precludes enforcement of patents on off-label uses and, by doing so, destroys the incentives for research into new uses of existing drugs—the principal area of innovation in the pharmaceutical industry today. The health of millions of Americans depends upon the proper resolution of the issue presented by this case. The stark division of opinion among the judges on a specialized court of appeals as to the proper interpretation of § 271(e)(2) cries out for this Court's review.

CONCLUSION

For the foregoing reasons, and those set forth in the petition, this Court should grant the petition for a writ of certiorari to the Federal Circuit.

Respectfully submitted,

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